**Appendix Table C2. Outcomes and interventions of studies that address Key Question 1**

| Study | Study Outcomes | Interventions |
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| Andratschke 2011, #132 | **Study Objective:** To report patterns of failure of SBRT in inoperable patients with histologically confirmed stage I NSCLC**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:** NA**List of Outcome(s):**OS, CSS, LCT, Toxicity**Cause of death:** Dead: 59 (64%)Dead due to LC: 25 (42%)Dead due to concurrent disease: 29 (49%)Cause of death NR: 5 (8%)**Length of FU:**21 (3-87) months | **Intervention name:**SBRT**Vendor name:**NR**Dose/frequency/details:** Hypofractionated SBRT Total dose: 24-45 Gy to 60% isodose line of PTV in 3-5 frs for 5-12 days Total dose given at 60% isodose line (Gy): 37.5 (24-45)Dose given per fraction (Gy): 12.5 (5–15)No. of frs given: 3 (3-7)**Technical details:** None**Treatment Intention:** Curative**Follow-up and Evaluation Criteria:** * All time intervals were calculated from the last day of SBRT
* During Rx, Patients monitored daily for acute Rx toxicity. Thereafter, follow-up visits at 4–6 weeks and 4, 7, and
* 12 months and then at 6 month intervals.
* FU investigations included lung function test and CT thorax.
* Acute toxicity: CTCAE v3.0 criteria during and up to 3 months after RT.
* Late toxicity: RTOG/EORTC criteria.
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| Baumann-2006, #271 | **Study Objective:** To review results of SBRT treatment of 138 Patients with medically inoperable stage I NSCLC treated during 1996 - 2003 at five different centers in Sweden and Denmark.**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:** NA**List of Outcomes:**LCT, OS, CSS, Toxicity**Cause of death:**Dead: 91 (66%)Dead due to concurrent disease: 55 (60%) Cause of death NR: 36 (40%)**Length of FU:**33 (1-107) months | **Intervention name:**SBRT**Vendor name:**NR**Dose/frequency/details:**10 to 20 Gy X 2-4 frs given 2 to 3 days apart.Total dose: 30-48 Gy, 65% isodose at the periphery of PTV**Technical details:**3D planningLinear accelerator delivered at 6-MV**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** Response is based on CT-scans performed in a period of 0.589.3 months (median 16.3) post therapy, and should therefore be regarded as ‘‘best response.’’
* Toxicity evaluated according to RTOC criteria
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| Baumann-2009, #270  | **Study Objective:** To evaluate the impact of COPD and CVD on Patients treated in this phaseII study, subjective toxicity data were registered during follow-up and compared to the objective data of spirometry evaluations, CT-scans and dosimetric data (#269).**Primary outcome:** Progression-free survival at 36 months**Definition:** NR**Secondary outcome(s):** LCT, OS, Toxicity**Definitions:** NR**Cause of death:** Dead: 27 (47%)Dead due to LC: 7 (26%) Dead due to concurrent disease: 18 (67%) Cause of death unknown: 2 (7%)**Length of FU:**Median: 35 months (4-47) | **Intervention name:**SBRT**Vendor name:**NR**Dose/frequency/details:**15 Gy in 3 frs (total dose of 45 Gy) at the 67% isodose of the PTV. BED: 112 Gy. Rx was given every second day.**Technical details:** 3DCT planningLinear accelerator delivered at 6-MV**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** Clinical, pulmonary and radiological evaluations- 6 weeks, 3, 6, 9, 12, 18, and 36 months post SBRT.
* Median FU time was calculated from date of registration to date of last visit
* Toxicity CTCAE version 2
* Radiation-related pulmonary ﬁbrosis >90 days post-Rx, RTOG/EORTC Late Radiation Morbidity Scoring Scheme-Lung was used
* FEV1 was graded according to the GOLD criteria
* Early toxicity defined as ≤ 18 months. Late toxicity defined as > 18 months
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| Bogart-2010, #382 | **Study Objective:** To deﬁne the maximally accelerated course of conformal radiotherapy and to describe the short-term and long-term toxicity of therapy.**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:** NA**List of outcomes:** OS, LCT, Toxicity**Cause of death:** NA**Length of FU:**53 (35-61) months | **Intervention name:**3DRT**Vendor name:**NR**Dose/frequency/details:**Daily radiation fraction size was escalated and the number offrs reduced. Total nominal radiotherapy dose maintainedat 70 Gy throughout each course. Treatment administered on consecutive weekdays.Range N of frs: (17 – 29)Range fraction size (Gy): (2.41-4.11)Range N of weeks: (3.4 – 5.8)**Technical details:** 3D planningBeam energy: (4 -25) MV83% treated with 6MV photons**Treatment Intention:**NR**Follow-up and Evaluation Criteria:*** Overall survival was deﬁned as the time between protocol registration and death
* Toxicity was assessed using the NCI CTC (version 2.0)
* Patients were assessed weekly during therapy. Patients were assessed 3 weeks, 6 weeks, and 3 months after the completion of therapy, then at least every 3 months for 2 years, and then every 6 months for 3 years.
* Evaluation by a thoracic surgeon (for suitability for lobectomy) was mandated if criteria for pulmonary dysfunction were not met,
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| Bollineni-2012, #4548 | **Study Objective:** To investigate the prognostic value of FDG-PET uptake at 12 weeks after SBRT for stage I NSCLC**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:** NA**List of Outcome(s):**OS, CSS, LCT**Cause of death:** Dead: 29 (22%)Dead due to LC: 13 (45%)Dead due to concurrent disease: 16 (55%)**Length of FU:**17 (3-40) months | **Intervention name:**SBRT**Vendor name:**Novalis-BrainLAB system (Westchester, IL) **Dose/frequency/details:** Hypofractionated SBRT Total dose: 60 Gy to 90% isodose line of PTV in 3-8 frs for 5-12 days **Technical details:** 4-D CT planning **Treatment Intention:** Curative**Follow-up and Evaluation Criteria:** NR |
| Bradley-2003, #445 | **Study Objective:** To review the outcome for 56 Stage I non–small-cell lung cancer treated deﬁnitively with three dimensional conformal radiotherapy (3D-CRT) and to investigate the value of elective nodal irradiation in this patient population.**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:** NA**List of outcomes:** OS, LCT, Toxicity**Cause of death:** NA**Length of FU:**20 (6 – 72) months | **Intervention name:**3DRT**Vendor name:**NR**Dose/frequency/details:**60–69 Gy: 7 (13%)70 Gy: 23 (42%)>70 Gy: 25 (45%)Median isocenter dose: 70 Gy (59.94 - 83.85), frs of 1.8 or 2 Gy, given 5 days weekly within 6 – 8 weeks.Twenty-two patients received RT directed to elective regional lymphatics in doses of 45–50 Gy**Technical details:** 3D planning**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** RTOG criteria used to evaluate toxicity grade 1-5 patients were followed at 3-month intervals for the ﬁrst 2 years and at 6-month intervals thereafter.
* Evaluations at the time of follow-up consisted of a history and physical examination. Chest radiographs were done at 3- or 6-month intervals for the ﬁrst 2 years. CT scans of the chest were typically done 6 and 12 Months after treatment completion and thereafter only when clinically indicated.
* Patients who had an initial radiographic response to treatment and a stable mass at each follow-up visit were considered to have local control.
* Patients were considered to have local failure only if clinical, radiographic, or biopsy evidence of progression was observed
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| Burdick-2010, #521 | **Study Objective:** To determine whether the pretreatment SUVmax from the staging FDG PET/CT could predict for mediastinal failure, distant metastases, and OS in medically inoperable patients treated with SBRT for early-stage NSCLC. To “deﬁne the maximal accelerated course of therapy”**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:** NA**List of outcomes:** OS, LCT**Cause of death:** Dead: 30 (42%)Dead due to LC: 13 (43%)Dead due to concurrent disease: 14 (47%)Causes of death unknown: 3 (10%)**Length of FU:**16.9 (0.1 – 37.9) months | **Intervention name:**SBRT**Vendor name:**Novalis-BrainLAB system (Westchester, IL) **Dose/frequency/details:**Total dose: 60 Gy (20 Gy X 3): 26 (36%)50 Gy (10 Gy X 5): 40 (56%)50 Gy (5 Gy X 10): 8 (11%)**Technical details:** 3D planning6-MV photons**Treatment Intention:**NR**Follow-up and Evaluation Criteria:*** Patients were followed every 3 Months with clinical examination and CT scan of the chest. Pulmonary function testing was done at 6-month intervals. Post-treatment PET scans were only performed to evaluate possible recurrences and are not included in this analysis.
* Local failure was dated from the initial CT abnormality. Local failure was deﬁned as increasing lesion size on two consecutive CT scans, conﬁrmed by serial PET imaging with or without positive biopsy for carcinoma.
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| Bush-2004, #535 | **Study Objective:** To determine the efficacy and toxicity of high-dose hypofractionated PBRT for Patients with clinical stage I lung cancer.**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:** NA**List of Outcomes:**CSS, LCT, OS, Acute Toxicity**Cause of death:**NR**Length of FU:**Median: 30 months | **Intervention name:**PBRT**Vendor name:**NR**Dose/frequency/details:**51 CGE in 10 equally divided frs over 2-weeks: 22 (32%)60 CGE in 10 frs over 2-weeks: 46 (68%)**Technical details:**Hypofractionated3D planningLinear accelerator delivered at 6-MV**Treatment Intention:**NR**Follow-up and Evaluation Criteria:*** Patients received clinical evaluation every 3 months for the first year, then every 6 months, then annually after the fifth year.
* Chest CT scans to determine tumor status were done at 3-month intervals up to 1 year after treatment, then every 6 months, and annually after the fifth year of follow-up.
* Patients were monitored weekly for acute toxicity during treatment.
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| Campeau-2009, #565 | **Study Objective:** To review retrospectively disease control and survival in patients with Stage I NSCLC patients who were treated with chemoradiotherapy or RT between 2000 and 2005.**Primary outcome:** OS**Definition:** OS was measured from treatment starting date to the date of death,regardless of the cause of death**Secondary outcome(s):** LCT, Distant LCT, and PFS**Definitions:** NR for LCT**List of outcomes:** OS, LCT**Cause of death:** NR**Length of FU:**NR | **Intervention name:**3DRT**Vendor name:**NR**Dose/frequency/details:**60 Gy X 30 frs over 6 weeks: 23 (68%)Hypofractionated dose: 50-55 Gy X 20 frs over 4 weeks: 11 (32%)The hypofractionated regimen was used only in cases in which the mediastinum and spinal cord were not included in the treatment volume.**Technical details:** ≥6-MV photons**Treatment Intention:**NR**Follow-up and Evaluation Criteria:*** Patients were seen every 3 months after completion of treatment for the ﬁrst 2 years. The interval was usually increased to every 6 months provided there was no evidence of recurrence.
* Chest X-ray or CT scan of the chest and upper abdomen were performed before each visit in most cases. An F-18 FDG PET scan was performed in case of equivocal CT scan results
* Local progression of (LCT) was defined per the RECIST criteria
* Local PFS was not censored by distant progression
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| Coon-2008, #803 | **Study Objective:** To assess the outcomes of Patients treated with stereotactic body radiation therapy (SBRT) in Patients with primary, recurrent, or metastatic lung lesions, with a focus on positron emission tomography (PET)/computed tomography (CT)–based management.**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:** NA**List of Outcomes:**LCT, OS**Cause of death:**NR**Length of FU:**Median: 12 months | **Intervention name:**SBRT**Vendor name:**NR**Dose/frequency/details:**60 Gy X 3 frs prescribed to the 80% isodose line**Technical details:**CyberKnife® Robotic Radiosurgery System with Synchrony™Linear accelerator delivered at 6-MV**Treatment Intention:**NR**Follow-up and Evaluation Criteria:*** All Patients received regularly scheduled follow-up with planned CT or PET-CT imaging per standard protocol.
* Local control was defined in our study as the lack of disease progression or reduction of standardized uptake value (SUV) at the site treated on follow-up imaging.
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| Dunlap-2010, #1032 | **Study Objective:** The purpose of this study was to compare the outcomes and local control rates of Patients with peripheral T1 and T2 non–small-cell lung cancer treated with stereotactic body radiation therapy.**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:** NA**List of Outcomes:**LCT, OS, Toxicity**Cause of death:**No treatment related deaths occurred**Length of FU:**12.5 (2-35) months | **Intervention name:**SBRT**Vendor name:**NR**Dose/frequency/details:**Median prescribed dose: 60 Gy (30-60 Gy) in 3 to 5 frsMedian BED: 150 Gy (78-180 Gy)**Technical details:**3D planning**Treatment Intention:**NR**Follow-up and Evaluation Criteria:*** After SBRT, followup was performed approximately 4 to 8 weeks after treatment and approximately every 3 months thereafter. CT of the chest was routinely obtained at 3-month intervals from the completion of radiotherapy. PET–CT was not routinely obtained before the initiation of therapy.
* Toxicity was graded using CTCAE version 3.0
* Local tumor recurrence was deﬁned as a 20% increase in the largest tumor diameter on successive follow-up imaging at 3-month intervals based on RECIST.
* Local recurrences were demonstrated by an increase in abnormal FDG uptake required to correspond to an enlarging CT abnormality.
* Follow-up was determined from the date of the final SBRT treatment.
* Guidelines for inoperability were determined by the thoracic surgeon and typically included a predicted postoperative forced expiratory volume in 1 second of less than 30%, severely reduced diffusion capacity greater 40% predicted, a performance status of 3 or greater, or severe cardiac disease.
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| Fritz-2008, #1238 | **Study Objective:** To review response rates, local control, survival and side effects after nonfractionated stereotactic high single-dose body radiation therapy for lung tumors.**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:** NA**List of Outcomes:**LCT, OS, Lung function, Toxicity**Cause of death:**Dead: 18 (45%)Dead due to LC: 13 (72%) Dead due to concurrent disease: 5 (28%) **Length of FU:**20 (6-61.5) months | **Intervention name:**SBRT**Vendor name:**NR**Dose/frequency/details:**BED 90% isodose: 99.9 Gy**Technical details:**4D Planning**Treatment Intention:**NR**Follow-up and Evaluation Criteria:*** All of the Patients were checked using high-resolution helical CT scans of the entire lung at 6 and 12 weeks after the single-dose radiation treatment. For all Patients further CT scan follow-up examinations then took place in 3-month intervals.
* The follow-up periods for overall and lung cancer speciﬁc survival were deﬁned as the time between irradiation and the last contact (censored) or death. No patient dropped out of follow-up. This means all Patients could be observed until the date of evaluation or the occurrence of an event.
* RTOG criteria used to evaluate toxicity
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| Graham-2006, #1403 | **Study Objective:** To review results of radical radiotherapy with 3DRT in Sydney to inform Patients contemplating treatment options for early stage NSCLC. **Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:** NA**List of outcomes:** OS, CSS, toxicity**Cause of death:** Dead: 22 (56%)Dead due to LC: 12 (55%)Dead due to concurrent disease: 10 (45%)**Length of FU:** Mean 40 (11-88) months | **Intervention name:**3DRT**Vendor name:**NR**Dose/frequency/details:**Prescribed dose: 65 Gy35 frs using concurrent end-phase boost5 weeks **Technical details:** 3D PlanningDelivered: 45 Gy in 25 frs plus 20 Gy in 10 frs concurrently during the last 2 weeks of treatment, with a 6-hour interfraction interval**Treatment Intention:** Curative**Follow-up and Evaluation Criteria:** NR |
| Iwata-2010, # 1747  | **Study Objective:** To analyzed the safety and efficacy of high-dose proton therapy and carbon-ion therapy applied to stage I NSCLC**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:** NA**List of Outcome(s):** OS, DSS, Local control, Toxicity**Cause of death:** NR**Length of FU:** All patients observed for a minimum of 1.5 years or until death. Median duration of follow-up was 35.5 (18-66) months for living pts & 30.5 (4-66) months for all pts. | **Intervention name:**PBRT**Vendor name:**Synchrotron (Mitsubishi Electric Corporation, Kobe, Japan3-D Rx planning system ((FOCUS-M, CMS, St. Louis, Mo and Mitsubishi Electric Corporation)**Dose/frequency/details:**PBRT 80Gy: 20 fractions, BED 10(Gy): 112PBRT 60 Gy: 10 fractionsBED 10(Gy): 96**Technical details:** Ptswere treated with 150-MeV proton beams **Treatment Intention:** NR**Follow-up and Evaluation Criteria:*** After Rx, pts FU at 1.5, 3, 4.5, 6, 9, and 12 months during the 1st yr, at intervals of 3 months in the 2nd yr, and at 6-month intervals in the 3rd yr.
* CT, tumor marker, Brain MRI and FDG-PET were used to monitor tumor progression.
* Local responses was assessed according to the modified WHO response evaluation criteria.
* Toxicities were evaluated with the CTCAE version 3.0.
* Medically inoperability defined as pts with poor pulmonary function (vital capacity <75% or ratio of FEV 1 to forced vital capacity <60%), a history of major CVD, severe DM, advanced age (80 years old), or other debilitating conditions that preclude surgery.
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| Jimenez-2010, #1842 | **Study Objective:** To assess clinical outcomes of high-dose accelerated 3DRT in medically inoperable patients with primary stage I NSCLC**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definition:**NA**List of outcomes:**OS**Cause of death:** NR**Length of FU:**36 months | **Intervention name:**3DRT**Vendor name:**XiO treatment planning system, Computer Medical System, Inc.Linear accelerator: Elekta SL15, Elekta, Crawley, OK, or Siemens Oncor, Siemens Medical Solutions, Concord, CA **Dose/frequency/details:**Individual dose-escalation scheme to maximal allowed total tumor dose of 79Gy in twice daily (BID) frs of 1.8 Gy with interfraction interval of at least 8 hours**Technical details:** 3D planningBeam energy NR**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** Survival status of the patients (alive or dead by any cause) was

evaluated in July 2009 in both series of cases* Follow-up was done by the Pulmonologist and/or Radiation Oncologist according to the national guidelines. Survival was updated using the ‘‘Gemeentelijke Basis Administratie” system, a decentralized population registration system containing information about all inhabitants of The Netherlands.
* During radiation treatment, patients were seen weekly by the Radiation Oncologist to treat the radiation-related complaints. (Details of complaints not specified)
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| Kopek-2009, #2040 | **Study Objective:** To determine the prognostic role of co-morbidity in medically inoperable patients with stage I NSCLC treated with SBRT**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definition:**NA**List of outcomes:**OS, CSS, LCT, toxicity**Cause of death:** NR**Length of FU:**44 (2-96) months | **Intervention name:**SBRT**Vendor name:**Treatment planning system: MDS\_Nordion, Freiburg, GermanyHelax-TMSCadPlan Plus/Eclipse, Varian Medical Systems, Palo, Alto, CALinear accelerator:Siemens Primus, Siemens Medical Solutions, Concord, CAVarian Clinac 2100/2300**Dose/frequency/details:**Prescribed dose: 45 or 68 Gy to PTV 95% isodose line3 frs5-8 days**Technical details:** Beam energy 6- or 8-MeV **Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** Clinical FU and CT scan at 3, 6, 9, 12, 24 months then annually after SBRT
* Toxicity assessed according to CTCAE v.3.0 criteria; Only deteriorations from baseline were registered as adverse events.
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| Mirri-2009, #2576 | **Study Objective:** To report on the clinical outcome of hypofractionated conformal radiotherapy for medically inoperable stage I NSCLC < 5 cm in diameter**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definition:**NA**List of outcomes:**OS, LCT, toxicity**Cause of death:** Dead: 7 (47%) **Length of FU:**25 (4-46) months | **Intervention name:**3DRT**Vendor name:**Treatment planning system:ECLIPSE,v.6.2, Varian Associates, Palo Alto, CAPinnacle. V.7.4f, Philips Medical System, Best, Netherlands**Dose/frequency/details:**Prescribed dose: 40 Gy to the PTV 95% isodose lineBED: 72 Gy5 frs2.5 weeks**Technical details:** Beam energy 6-MeV **Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** CT scan at 4 months after 3DRT, then every 4 months thereafter
* Acute toxicity assessed according to RTOG criteria

Late toxicity assessed according to EORTC and CTCAE v.2.0 Data also evaluated by ECOG CTC criteria (both late and acute) |
| Nakayama-2010, #2684 | **Study Objective:** To evaluate the role of PBT for Patients with medically inoperable stage I NSCLC**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definition:** NA**List of outcomes:**OS, LCT, toxicity**Cause of death:**Dead due to LC: 0Dead due to concurrent disease: 2 (4%)**Length of FU:**18 (1.4-53) months | **Intervention name:**PBT**Vendor name:**PROBEAT, Hitachi, Tokyo**Dose/frequency/details:**Central Lesions: 73 GyE in 22 frs: 17 (29%)Peripheral Lesions: 66 GyE in 10 frs: 41 (71%)BED: 1.1**Technical details:** Beam energies 155-250 MeV**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** Monthly at completion of PBT for 6 months
* Chest CT every 3 months for 2 years after PBT Spirometry
* Toxicity scored according to CTCAE v3.0
* The local control rate for 58 tumors was calculated to the date of tumor size increase of >20%.
* Survival rates were calculated from the ﬁrst day of treatment with PBT
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| Narayan-2004, #2686 | **Study Objective:** To evaluate clinical outcomes of dose escalated 3DRT in medically inoperable patients with NSCLC**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definition:**NA**List of outcomes:**OS, CSS**Cause of death:** Dead: 12 (80%)Dead due to LC: 4 (33%)Dead due to concurrent disease: 8 (67%)**Length of FU:**NR | **Intervention name:**3DRT**Vendor name:**NR**Dose/frequency/details:**Prescribed dose: 92 (N=7 (54%)) or 103 Gy (N=6 (46%)) to PTV 95% isodose line2.1 Gy fraction dailyOnce per day, 5 days per week**Technical details:** Beamenergy NR**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** 1 month after 3DRT, every 3 months for 2 years, every 4 months for the third year, every 6 months for the next 2 years, then annually
* Chest Xray every visit, CT scan every 6 months
* Toxicity assessed according to SWOG criteria
* Patients with disease visualized on bronchoscopy at diagnosis underwent repeat bronchoscopy at 6 months to evaluate local control.
* Overall survival (OS) was calculated from the date of the initiation of radiation to the date of death or last follow-up
* Deaths due to causes other than lung cancer were censored to determine cause speciﬁc survival (CSS)
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| Nyman-2006, #2750 | **Study Objective:** To determine clinical outcomes with SBRT in the treatment of stage I NSCLC in medically inoperable patients**Primary outcome:** NR**Definition:**NA**Secondary outcome(s):** NA**Definition:**NA**List of outcomes:**OS, CSS, toxicity**Cause of death:** Dead: 24 (53%)Dead due to LC: 15 (62%)Dead due to concurrent disease: 9 (38%) **Length of FU:**43 (24-74) months | **Intervention name:**SBRT**Vendor name:**CadPlan Treatment Planning System, Varian**Dose/frequency/details:**Prescribed dose: 45 Gy to the PTV 100% isodose line3 frs1 week**Technical details:** 6-MeV beam energy**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** 6 weeks, 3 months, 6 months, every 6 months thereafter
* Physical exam, performance status, toxicity assessed
* CT scan at all time points except 6 weeks
* Acute and late toxicity assessed according to EORTC/RTOG scoring system. The acute toxicity was registered during treatment or at the 6-week follow-up visit.
* Nine patients who died without tumor progression or metastases were censored at the time of deaths.
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| Olsen-2011, #2792 | **Study Objective:**To compare the efficacy of three lung SBRT regimens in a large institutional cohort**Primary outcome:**NR**Definition:** NA**Secondary outcome(s):** NR**Definition:**NA**List of outcomes:**OS, LCT, toxicity**Cause of death:** NR**Length of FU:**Median: 11, 13, 16 months for 3 dose groups | **Intervention name:**SBRT**Vendor name:**Pinnacle3 treatment planning system, Philips Medical**Dose/frequency/details:**Three prescribed dose regimens: Peripheral: 18 Gy X 3 frs = 54 Gy (N=111), Central: 9 Gy X 5 frs = 45 Gy (N=8) OR 10 Gy X 5 frs = 50 Gy (N=11)5 Patients received: 5 frs at incremental doses of 9, 10, 11, and 12 Gy9 Patients received: 9-10 Gy X 5 frs**Technical details:** 4D Planning6-MV photons8–11 beams**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** Duration NR
* CT imaging and physician visits
* Toxicity scored according to CTCAE v.3.0
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| Palma 2012, #2843 | **Study Objective:** To evaluate outcomes after SBRT in Patients with severe COPD**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:**NA**List of outcomes:**OS, LCT, toxicity**Cause of death:** Total: 62 (35%)Cause NR**Length of FU:**Median: 21 months | **Intervention name:**SBRT**Vendor name:**Brainscan v.5.2 treatment planning system, BrainLab, Feldkirchen, GermanyRapidArc linear accelerator, Varian, Palo Alto, CA **Dose/frequency/details:**Prescribed dose: BrainLab:3 x 20 Gy, 5 x 12 Gy, or 8 x 7.5 GyRapdArc: 3 x 18 Gy, 5 x 11 Gy, or 8 x 7.5 Gy80% PTV isodose line**Technical details:** 6-MV photons8–12 noncoplanar static beams**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** Outpatient assessments at 3-6 month intervals post-SBRT
* Diagnostic CT scan at each visit
* Toxicity assessed according to CTCAE v.3.0
* Late toxicity defined as >6 weeks after treatment
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| Pennathur-2007, #2896 | **Study Objective:** To evaluate CT-guided RFA as an alternative treatment option for high-risk medically inoperable patients with stage I NSCLC **Primary outcome:** NR**Definition:**NA**Secondary outcome(s):** NR**Definition:**NA**List of outcomes:**OS, complications**Cause of death:** Dead: 6 (33%)Dead due to LC: 3 (50%)Dead due to concurrent disease: 2 (33%)Causes of death unknown: 1 (17%)**Length of FU:**28 (9-52) months | **Intervention name:**RFA**Vendor name:**Generator:RF3000, Boston Scientific, Boston, MARITA Starburst XL, RITA Medical SystemsNeedle electrodes:LeVeen, Radiotherapeutics Corporation, Sunnyvale, CAStarburst XL, RITA Medial Systems**Dose/frequency/details:**RF3000: power 5-10W increments until system impedance > 400 ohmRITA: power 35-50 W, target temperature 90 degrees C**Technical details:** With both systems, electrode was repositioned as many times as needed to encompass the target tissue and a small rim of about 0.5-1.0 cm nondiseased tissue**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** 3-month intervals
* Clinical examination, CT and selective FDG PET scans
* Modiﬁed RECIST criteria were used to assess initial response to treatment at 3 to 5 months
* The time to progression was calculated from the treatment date.
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| Pennathur-2009, #2898 | **Study Objective:** To determine the outcomes of SRS in the treatment of stage I NSCLC.**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definition:**NA**List of outcomes:**OS, complications**Cause of death:** Total: 10 (48%) cause not specified**Length of FU:**21 (12-43) months | **Intervention name:**SBRT**Vendor name:**Cyberknife, Accuray, Sunnyvale, CA**Dose/frequency/details:**HypofractionatedPrescribed dose: 20-60 Gy to the 80% PTV isodose lineBED: 60-70 Gy1-3 frs**Technical details:** 6-MeV beam energy**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** 3-month intervals with CT and FDG PET scans
* Modiﬁed RECIST criteria were used to assess initial response to treatment at 3 months
* The time to progression was calculated from the treatment date after censoring data from patients who died without progression.
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| Ricardi-2010, #3098 | **Study Objective:** To evaluate clinical outcomes and toxicity of SBRT in Patients with stage I NSCLC who were medically inoperable or refused surgery**Primary outcome:** LCT**Definition:** LCT defined as absence of local failure, diagnosed as tumor growth or re-growth after initial shrinkage**Secondary outcome(s):** OS, CSS, toxicity**Definitions:** OS defined as death from any cause after SBRTCSS defined as death due to cancer after SBRT **List of outcomes:**OS, CSS, LCT, toxicity**Cause of death:** Dead: 20 (32%)Dead due to LC: 12 (60%)Dead due to concurrent disease: 8 (40%)**Length of FU:**28 (9-61) months | **Intervention name:**SBRT**Vendor name:**Oncentra OTP 3D treatment planning system, Nucletron, NetherlandsElekta Precise linear accelerator, Elekta, Netherlands**Dose/frequency/details:**Prescribed dose: (15 Gy x3) 45 Gy to 80% PTV isodose lineBED: 124 Gy3 frs1 week**Technical details:** 6–10 MV photons6–8 noncoplanar static beamsAverage time for a single session was approximately 45 min**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** 6 weeks, then every 3 months after SBRT
* Clinical examination and CT scans
* Acute and late toxicity assessed according to RTOG criteria
* Late toxicity defined as: events occurring after day 90
* Acute toxicity defined as: events occurring between day 1 and

day 90 from the start of radiation treatment* RECIST criteria used to evaluate tumor response
* Local tumor control was deﬁned as absence of local failure,

diagnosed as tumor growth or re-growth after initial shrinkage.Overall survival started from time of SBRT until death from any cause |
| Scorsetti-2007, #3362 | **Study Objective:** To determine clinical outcomes with SBRT in the treatment of stage I NSCLC in medically inoperable patients**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definition:**NA**List of outcomes:**OS, LCT, toxicity**Cause of death:**Dead: 10 (23%)Dead due to LC: 2 (20%)Dead due to concurrent disease: 8 (80%)**Length of FU:**14 (6-36) months | **Intervention name:**SBRT**Vendor name:**Ergo TPS treatment planning system**Dose/frequency/details:**Prescribed dose: 20-32 GyBED: 40-117 Gy7-10 Gy per fraction2-4 frs**Technical details:**Beam strength NR **Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** 45 days, then every 3 months after SBRT
* CT scans, spirometry
* Toxicity assessed according to RTOG/EORTC criteria
* 3 months= acute toxicity after radiotherapy and after 3 months =late toxicity.
* Local progression defined as: increase of tumor volume

of more than 25% in volume in CT scan and/or increased uptake inPET |
| Shibamoto -2012,#4629 | **Study Objective:** To report a multi-institutional study of SBRT in inoperable and operable patients with histologically confirmed stage I NSCLC**Primary outcome:** LC at 3-years follow-up**Definition:** Calculated from the start of SBRT**Secondary outcome(s):** OS, CSS**Definitions:** Calculated from the start of SBRT**List of Outcome(s):**OS, CSS, LCT, Toxicity**Cause of death:** Dead: 65 (36%)NR by operability**Length of FU:**36 monthsNR by operability | **Intervention name:**SBRT**Vendor name:**Novalis image-guided system (Varian Medical Systems, Palo Alto, CA)CLINAC 23EX or 21 EXS (Varian)Eclipse v.7.5.14.3 (Varian)BRAINSCAN v.5.31 (BrainLAB, Feldkirchen, Germany)Pinnacle3 (Philips, Madison, WI)**Dose/frequency/details:** Hypofractionated SBRT Total dose: 44-52 Gy to 90% of the isodose line of PTV in 4 frs for 9-21 days **Technical details:** 6-MV photons**Treatment Intention:** Curative**Follow-up and Evaluation Criteria:** * All time intervals were calculated from the start of SBRT
* CT scans of chest and upper abdomen at 2-months intervals up to 6 months, every 2-4 months thereafter
* Toxicity: CTCAE v3.0 criteria during and up to 3 months after RT
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| Song-2009, #3549 | **Study Objective:** To evaluate clinical outcomes and toxicity of SBRT as treatment for Patients with primary Stage I NSCLC adjacent to central large bronchus and who are medically inoperable or refuse surgery**Primary outcome:** NR**Definition:**NA**Secondary outcome(s):** NR**Definitions:** NA**List of outcomes:**OS, LCT, toxicity**Cause of death:**NR**Length of FU:**26 (5-92) months | **Intervention name:**SBRT**Vendor name:**Render 3-D treatment planning system, Elekta Oncology, NetherlandsEclipse treatment planning system, Varian USA**Dose/frequency/details:**Prescribed dose: 40-60 Gy to 85% PTV isodose line3-4 frs10-20 Gy per fraction3-4 consecutive days**Technical details:** 3D PlanningBeam energy NR**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** 1, 6, 12 months after SBRT
* Chest CT
* Pulmonary toxicity scored by NCI-CTC v. 2.0
* Local tumor control was deﬁned as a tumor response of stable disease (SD) or better.
* Radiation-induced bronchial stricture was initially determined on scheduled follow-up CT scans or simple Chest X-ray by narrowing of bronchus or secondary collapsed lung parenchyma. Some Patients were observed with only follow-up CT scans without additional examination if the radiation-induced stricture was stable.
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| Stephans-2009, #3614 | **Study Objective:** To assess the impact of fractionation upon tumor control and toxicity in medically inoperable early stage lung cancer patients treated with SBRT**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definition:**NA**List of outcomes:**OS, LCT, toxicity**Cause of death:** Dead: 25 (29%)**Length of FU:**15 (2-48) months | **Intervention name:**SBRT**Vendor name:**BrainScan 5.31 treatment planning system, BrainLAB, Feldkirchen, GermanyNovalis linear accelerator, BrainLAB**Dose/frequency/details:**Two fractionation schemes:60 Gy to 81-90% isodose line3 frs8-14 days50 Gy to 97-100% isodose line5 frs5 days**Technical details:** 6-MeV beam energy**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** 6-8 weeks after SBRT, every 3 months thereafter with CT and pulmonary function test twice annually
* Toxicity assessed according to CTCAE v.3.0
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| Taremi-2011, #3732 | **Study Objective:** To present the results of SBRT for medically inoperable patients with stage I NSCLC and contrast outcomes in patients with and without a pathologic diagnosis**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definition:**NA**List of outcomes:** OS, CSS, LCT, toxicity**Cause of death:** Dead: 45 (42%)Dead due to LC: 17 (38%)Dead due to concurrent disease: 28 (62%)**Length of FU:**19 (1-56) months | **Intervention name:**SBRT**Vendor name:**Pinnacle treatment planning system, Philips, Madison, WILinear accelerator NR**Dose/frequency/details:**Prescribed dose: 48-60 Gy to the PTV 90% isodose line3-10 frsDaily fractionation for some regimens, duration NR for all regimens**Technical details:** Beam energy NR**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** 6 weeks after SBRT, then every 3 months for first year, every 6 months in second year, annually thereafter
* FDG PET at 3 months after SBRT
* CT at 6 and 12 months after SBRT, every 6-12 months thereafter
* CTCAE v 3.0
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| Takeda-2009, #3700 | **Study Objective:** To analyze clinical outcomes of SBRT for patients with stages IA and IB NSCLC**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definitions:** NA**List of outcomes:**OS, CSS, LCT, toxicity**Cause of death:** NR**Length of FU:**31 (10-72) mos | **Intervention name:**SBRT**Vendor name:**XiO treatment planning system, V.4.2 or v.4.3, CMS, St. Louis, MOLinear accelerator NR**Dose/frequency/details:**Prescribed dose: 50 Gy to the 80% isodose line10 Gy per fraction5 fractions**Technical details:** Beam energy NR**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** Monthly for first 6 mos, with chest X-ray
* CT scans at 1 and 3 mos after SBRT, then at 3-mos intervals during first 2 years
* FU interviews and CT scans at 4-6 mos intervals after 2 years
* Toxicity assessed according to CTCAE v.3.0
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| Turzer-2011, #3842 | **Study Objective:** To assess SBRT results and toxicity for stage I NSCLC Patients with low performance status and severe comorbidity**Primary outcome:** NR**Definition:**NA**Secondary outcome(s):** NR**Definitions:** NA**List of outcomes:**OS, LCT, toxicity**Cause of death:** Dead: 1 (3%)**Length of FU:**14 (0-21) months | **Intervention name:**SBRT**Vendor name:**Elekta Synergy linear accelerator, Elekta AB**Dose/frequency/details:**Prescribed dose: 45 Gy to PTV 100% isodose line3 frs1 week**Technical details:** Beam energy NR**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** 6 weeks, 3, 6 months after SBRT. Every 6 months thereafter
* Physical examination and chest CT every visit, FDG PET twice annually
* Toxicity assessed according to CTCAE v.3.0 criteria
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| Vahdat-2010, #3864 | **Study Objective:** To report serial FGD PET/CT tumor response following Cyberknife radiosurgery for stage IA NSCLC in inoperable patients**Primary outcome:** NR**Definition:** NA**Secondary outcome(s):** NR**Definition:**NA**List of outcomes:**OS, LCT**Cause of death:** Dead: 3 (15%)Dead due to concurrent disease: 3 (100%)**Length of FU:**43 months | **Intervention name:**SBRT**Vendor name:**Cyberknife, Accuray**Dose/frequency/details:**Prescribed dose: 42-60 Gy to PTV 95% isodose line3 frs**Technical details:** Beam energy NR**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** FDG PET at 3-6, 9-15, 18-24 months after SBRT
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| van der Voort van Zyp-2009,#3885 | **Study Objective:** To report the clinical outcome of treatment using real-time tumor tracking for 70 Patients with inoperable stage I NSCLC**Primary outcome:** LCT, OS, CSS**Definition:** LCT: Calculated from first day of treatment until diagnosis of local recurrenceOS: measured from start of SBRT until death from any causeCSS: measured from start of SBRT until death from lung cancer**Secondary outcome(s):** NR**Definitions:** NA**List of outcomes:**OS, CSS, LCT**Cause of death:** Dead: 19 (27%)Dead due to LC: 6 (32%)Dead due to concurrent disease: 13: (68%)**Length of FU:**Median 15 months | **Intervention name:**SBRT**Vendor name:**On Target treatment planning system, v.3.4.1, Accuray, Sunnyvale, CACyberknife Synchrony RTS linear accelerator, Accuray**Dose/frequency/details:**Prescribed dose: 36-60 Gy to the PTV 70-85% isodose line3 frsDuration NR**Technical details:** Beam energy NR**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** Clinical examination and chest CT 3 weeks, 2-3, 6, 9, 12, 18, 24, 30 months thereafter
* Toxicity assessed according to CTCAE v.3.0 criteria
* Toxicity was acute if it occurred within 4 months and late if it occurred thereafter
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| Videtic-2010, #3958 | **Study Objective:** To validate the use of SBRT using IMRT beams for medically inoperable stage I NSCLC**Primary outcome:** OS, LCT**Definition:** Measured from time of diagnosis until death or last patient contact**Secondary outcome(s):** NR**Definition:**NA**List of outcomes:**OS, LCT, toxicity**Cause of death:** Dead: 14 (54%)Dead due to LC: 8 (57%)Dead due to concurrent disease: 6 (43%)**Length of FU:**31 (10-51) months | **Intervention name:**SBRT with IMRT beams**Vendor name:**Novalis-BrainLAB treatment system**Dose/frequency/details:**Prescribed dose: 50 Gy to the 95% isodose line5 frs5 days**Technical details:** Beam energy NR**Treatment Intention:**Curative**Follow-up and Evaluation Criteria:*** Initially 6-8 weeks after SBRT, every 3 months for 2 years thereafter
* Chest CT scan at each visit with same-day pulmonary function test twice annually
* Toxicity assessed according to CTCAE v.3.0 criteria
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